MEDICAL RESEARCH COUNCIL

Thyroid Enlargement and other Changes Related to the Mineral Content of Drinking Water

(With a Note on Goitre Prophylaxis)

PRIVY COUNCIL

MEDICAL RESEARCH COUNCIL MEMORANDUM

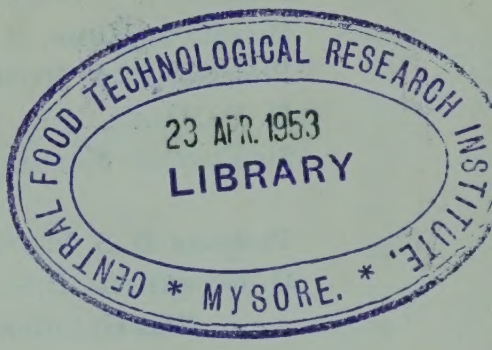
No. 18

THYROID ENLARGEMENT AND OTHER CHANGES RELATED TO THE MINERAL CONTENT OF DRINKING WATER

(WITH A NOTE ON GOITRE PROPHYLAXIS)

by

Margaret M. MURRAY, J. A. RYLE
Beatrice W. SIMPSON and Dagmar C. WILSON



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THYROID ENLARGEMENT AND OTHER BODILY CHANGES RELATED TO THE MINERAL CONTENT OF DRINKING WATER

by

Margaret M. Murray, D.Sc., J. A. Ryle, M.D., F.R.C.P.,
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INTRODUCTION

In the course of nutritional surveys in Oxfordshire made early in the war by Dr. D. C. Wilson, an unusually high incidence of goitre was brought to light by clinical examination of housewives and of women engaged in industry. At the same time investigation of endemic fluorosis among school-children in the villages of North Oxfordshire, undertaken with Professor M. M. Murray on behalf of the Medical Research Council, revealed a relatively high incidence of thyroid enlargement in the adolescent school-children in addition to indications of a mild degree of fluorosis affecting the teeth. The distribution of such abnormalities was found to correspond roughly with a low iodine and a high fluorine content of the drinking water. These studies, sponsored by the Lister Institute and the Medical Research Council, were later supported by the Oxford Institute of Social Medicine, where they were adopted as part of the official programme. The results were reported to the Accessory Food Factors Committee, which considered them important enough to warrant the formation in May 1943 of a Goitre Sub-Committee, under whose auspices the later work described in this report was carried out.

The investigations have been of a two-fold nature and have included: (1) clinical surveys of selected groups of individuals from chosen areas of the country in order to determine the incidence of thyroid enlargement, and (2) analysis of the drinking water of these areas for its mineral content. In areas where there had been no recent change in the sources of drinking water, the results of the present clinical examinations of children have usually confirmed the findings of the extensive survey to determine the incidence of thyroid enlargement carried out 20 years ago by the Board of Education, the results of which were later analysed by Stocks (1928). The high incidence of established goitre in certain districts where the iodine content of the water is low (under 3 μg. per litre) has indicated the need for extra provision of this element by the use of iodized salt, a recommendation already made by the Goitre Sub-Committee (1944), see p. 34.

The investigations which provide the clinical data for this report have been concerned chiefly with the relation of the thyroid hyperplasia seen in children and young adults in goitrous areas to that occurring in goitre-free areas. For the clinical assessment of the condition of the thyroid gland no satisfactory standard method was available. In Part I of this report, therefore, a description is given of a simple method which is easy to learn and to apply. This method has been used for all the surveys carried out during the present investigations.

The association of abnormalities of the thyroid with the iodine and mineral content of the drinking water has been re-investigated, in spite of much previous work in other countries, because we were not satisfied that in England the iodine level was the only determining factor in the drinking water. Furthermore, it was considered that observations on the iodine content of water made before the introduction of Harvey's method (1935) were not reliable. Young *et al.* (1936) showed that for two areas of England, one goitrous the other relatively goitre-free, the iodine level was not the only factor determining the degree of incidence of thyroid hyperplasia in children, but no suggestion was made as to the nature of any other factor or factors except to indicate that they were concerned with the soil or water. The goitrous area of Young's investigation was Somersetshire, long known for its record of goitre and cretinism. Observations by Wilson (1941) showed that dental fluorosis and goitre co-exist in that county, and the waters then in use were found to contain small amounts of fluorine and to be hard (Bromehead, Murray and Wilson, 1943). At the time of Young's survey (1936), the waters were very hard but many wells then in use have since been closed.

Although the association of goitre with hard waters and limestone regions has been frequently observed, no convincing evidence of a causal relationship has yet been offered. In the present investigation further evidence was sought by including measurements of calcium, magnesium and total hardness, as well as of iodine and fluorine, in samples of the drinking waters from the areas studied.

In all about 6,000 school-children of all ages were examined in 25 districts supplied with waters of high or low iodine content and of different degrees of hardness. Confirmation has been obtained of the well-known fact that the content of iodine in the water is a determining factor in the distribution of endemic goitre, but the present results show also that an iodine level which in a soft water may be adequate to prevent goitre may be insufficient where the water is hard.

The occurrence of cretinism and deaf-mutism in a low iodine area of England has also been studied.

The possibility that the fluorine content of the water might play a part in the causation of endemic goitre has also been investigated, but in Great Britain there are very few areas where the water contains more than 1 part per million of fluorine, and it is felt that this hypothesis should preferably be tested in areas where endemic fluorosis is more extensive and more severe.

The iodine contents of 81 English and Welsh waters, and of 64 Scottish waters, are given respectively in Tables V (p. 24) and VI (p. 25) of this report.

I.—CLINICAL ASSESSMENT OF THYROID ENLARGEMENT

BY

J. A. RYLE

Previous surveys

Difficulties inherent in the clinical appreciation of thyroid enlargement were experienced in the 1924 Board of Education survey, in which about 600 school medical officers took part, and a large personal equation was inevitable (Campbell, 1927). By the application of frequency curves obtained from actual measurements of the gland, Stocks *et. al.* (1927) calculated the range of error due to personal differences in estimation. Stocks (1928) recommended for future comparative work the use of a standard 42 mm. gauge for thyroid breadth, and concluded that up to a certain point all forms of simple thyroid enlargement increased in roughly the same proportion in passing from non-goitrous to goitrous districts. This suggested that the so-called "physiological goitres" differed from true endemic goitre only in stage or degree. Studies of geographical distribution in the light of the estimated probable errors indicated that goitre was more prevalent in girls than boys, but that the sex ratio fell rapidly from about 5 : 1 in areas almost free from goitre to one of 2 : 1 in districts where the incidence among boys (according to Stocks' definition of enlargement of the thyroid gland at the time of examination) was about 10 per cent., and then gradually reached unity in regions of high prevalence. According to the standards employed by the school medical officers, what may be described as a "residual" rate for thyroid enlargement was present even in areas of low incidence. This amounted to about 3 or 4 per cent. in girls and 0·5 to 1 per cent. in boys. Young *et al.* (1936) combined general inspection of the neck with the method of calliper measurement suggested by Stocks.

Doubts of the high incidence of "goitres" recorded in some school surveys were expressed by McCarrison (1933), who suggested a distinction between physiological and pathological enlargement. By following the ratio of thyroid weight to body weight throughout the life span of several species of animals, he found that the gland attains its maximum size just before the onset of sexual maturity. Means (1937) also concluded that a slight fullness of the thyroid at puberty may be normal, and minor adolescent enlargements without symptoms have commonly been accepted as "normal" by physicians of experience.

Definition of goitre

The word "goitre" should preferably be reserved for a gland which has become enlarged in the clinical sense, in greater or less degree, and has also undergone prolonged or permanent change. This report is not concerned with goitres accompanied by thyrotoxicosis, but with those types which are customarily described as "simple" or "endemic", to indicate, respectively, that they are uncomplicated by thyrotoxicosis and that they tend to have a geographical distribution. In England goitres of this type do not usually become manifest until adult life. They are seen in their full stage of development chiefly in women at or after 30 years of age. In areas of high endemicity, however, where goitre and cretinism have been common or still occur (Norris, 1848 ; Fagge, 1871), and in parts of the world where general nutrition is poor and water supplies show mineral deficiencies and are unprotected from pollution, established goitres may be seen even in childhood (McCarrison, 1928). Some simple goitres undergo nodular changes and may later give rise to secondary thyrotoxic manifestations in middle life with particular effects on the heart (Linnell *et al.*, 1946).

The term "goitre" has sometimes been further applied to other thyroid

enlargements, including the not infrequent enlargements occurring in adolescence, of which the majority are slight in degree and temporary, only a small minority later undergoing some permanent change. We are not yet certain whether the minor degrees of such enlargements should be considered to lie within physiological limits, or whether they should be regarded as early or minor manifestations of a pathological hyperplasia. The relation of iodine deficiency to such "thyroid enlargements of adolescence" is discussed on pp. 13 and 23.

Method of assessing size of thyroid gland adopted in present survey

The estimation of the size of an organ in life can never be exact, and the fact that the thyroid lies so near the surface does not make such estimations much easier or more accurate than those of the deep-seated viscera. Necks vary greatly in conformation, length and muscularity, and in the amount and distribution of the subcutaneous fat. These variants influence the visibility and palpability of the gland. The normal gland is soft and its shape, thickness, visibility and position can be modified by the position of the head, the degree of stretch of the neck muscles and fascia, and by the act of swallowing. Although changes in the size of established goitres have been studied in the individual by circumferential measurements, and attempts to grade the breadth of the gland with the use of callipers have been made in surveys of schoolchildren (Stocks *et al.*, 1927), the errors inherent in the judgment of the observer—which are increased wherever multiple observers working separately are concerned—and the variations in the posture of the subject and in the strength, development and direction of the overlying sterno-mastoid muscles must be considerable. For these reasons the following clinical method of grading and recording size and other changes, which does not entail instrumental measurement, would seem preferable.

All subjects should preferably be examined by two observers, in order to provide a check in cases of doubt or difficulty. They should come into the room with their necks bared and should be examined in good daylight, the examiner sitting with his back to the window with the subject facing him and seated on a swivel stool adjusted to an appropriate height.

In this position the neck is first inspected at rest and on swallowing with the head at a natural angle, the chin being neither unduly raised nor lowered. When the light behind the observer falls from above, a faint shadow is often seen between the lower limit of an enlarged thyroid gland—even when the enlargement is slight—and the suprasternal notch. Swallowing movements help to satisfy the examiner that an observed fullness does, in fact, correspond with the gland. Care should be taken to distinguish a prominent cricoid cartilage from the isthmus. The gland is next palpated in the region of the lateral lobes with the flat of the finger tips of both hands. The isthmus can be most conveniently palpated with the flat of the thumb, the fingers being placed behind the neck. The swivel stool is then turned and the neck is inspected in profile. In this view, true thyroid fullness appears as a gently rounded convexity of varying degree, in place of the more usual straight line from the laryngeal cartilages to the suprasternal notch. The stool is then turned further and the gland finally palpated from behind with the finger tips of both hands.

The glands are recorded as *invisible*, *visible*, or *visible* + (*the Rossetti neck*). Inspection on swallowing, palpation from in front and behind, and observation of the profile view, together help to distinguish fullnesses of the neck due to muscular development, to fat or to peculiar conformations, from those due to enlargement of the gland itself. Palpation also determines consistency and the presence or absence of asymmetry or nodular changes. The texture and form of the glands are recorded as *soft*, *smooth*, *symmetrical* or as *firm* (or *hard*),

Form for Recording the Results of the Examination of the Thyroid Gland

Place Hook Norton *Date* 29.iv.43.
School ,, ,,

No.	*Sex*	*Name*	*Age last birthday*	*Address*	*STATE OF GLAND*							*Grouping of gland*	*Remarks (previous residence, etc.)*
					visibility at rest	*soft*	*smooth*	*sym-metrical*	*firm*	*nodular*	*asym-metrical*		
1	Male	B.P.	12	Hook Norton	—	√	√	√				a (normal)	Resident since birth
2	Male	C.D.	11	Hook Norton	—	√	√	√				a (normal)	Resident since birth
3	Female	B.D.	15	Hook Norton	√		√	√	√			d (pathological)	Resident since birth; mother goitrous
4	Male	K.E.	10	Hook Norton	—	√	√	√				a (normal)	Resident since birth
5	Male	G.D.	13	Hook Norton	√		√	√	√			d (pathological)	Resident since birth
6	Female	W.J.	14	Hook Norton	√+	√	√	√				c ("Rossetti," or marked hyperplasia)	Resident 4 years
7	Female	G.M.	11	Hook Norton	—	√	√	√				a (normal)	Resident 7 years
8	Male	H.C.	11	Hook Norton	√	√	√	√				b (slight hyperplasia)	Resident since birth social conditions poor
9	Female	F.T.	13	Hook Norton	√	√	√	√				b (slight hyperplasia)	Resident since birth
10	Male	F.J.	14	Hook Norton	—	√	√	√				a (normal)	Resident since birth

asymmetrical, nodular. A simple record-sheet is used for noting the findings under the appropriate headings. A reproduction of the form used for records is given on p. 8 including typical examples of glands falling into the different groups.

As a result of the examination of many hundreds of subjects we are satisfied that useful assessments can be made by this method, and that with very few exceptions a gland examined in the course of a routine clinical survey of children and adolescents can be placed in one of the four following categories :

Group (*a*) Invisible at rest.

Group (*b*) Visible to the trained observer, but soft, smooth and symmetrical.

Group (*c*) Conspicuously enlarged (visible +), but showing no palpable asymmetry, firmness or nodular change. This type is sometimes referred to as the "Rossetti" neck.

Group (*d*) Showing a degree of firmness, asymmetry or nodular change, which can be regarded as definitely pathological.

Occasionally a firm isthmus may be found without other obvious changes in the gland. In a small proportion of cases a pea-like nodule in the centre of the isthmus, not apparently superimposed upon it, may be noted without other change ; possibly this may be a precursor of the solitary adenoma of the isthmus sometimes observed as a larger local swelling in the adult. These minor abnormalities are better excluded in any regional or community survey undertaken to discover the incidence of adolescent enlargements.

Surveys involving upwards of 4,000 school-children, aged from 11 to 17 years, in the English counties of Berkshire, Devon, Dorset, Essex and Oxford and in the Scottish counties of Dumfries and Inverness have been made by this method. The procedure is simple and the willing co-operation of school teachers and nurses can be relied upon. With practice two clinical observers, each examining every child, with one clerical assistant to record the findings on a prepared sheet, can together examine 80 to 100 children in an hour. Large-scale surveys of established goitre in adults are far more difficult to carry out owing to the inconvenience caused to householders by domestic visitations, the scatter of populations in rural areas, which are those principally affected, and the changes of habitation by individuals.

Significance of different types of enlargement

Most of the children examined fell into the category we have called Group (a) ; Groups (b) and (c) comprised the majority of those showing the "enlargement of adolescence" ; Group (d) cases were very scarce.

It is known that with the approach of maturity a natural increase in size of the thyroid occurs in mammals (McCarrison, 1928). The same enlargement occurs in the human species at puberty, especially in girls. Sigurjönsson (1940) gives a good resumé of observations on the relation between age and size of the thyroid gland in human beings. The biggest series of figures is that of Roessle and Roulet (1932) for Jena and Basle. All such data, with the exception of those for Iceland, when plotted as a curve of thyroid weight against age, show a steep rise in the curve up to the age of 20 years. The more goitrous the region, the steeper is the rise, showing that adolescent hyperplasia is greater where the incidence of established adult goitre is greater. From comparisons of the weights of kidneys, suprarenals, liver and pancreas in man, it is well known that the average weight of an organ in the male is greater than that of the corresponding organ in a female of the same age. It is therefore perhaps surprising that in many records one finds either a greater or an equal weight given for the thyroid in the female, as compared with that of the male (Roessle and Roulet, 1932 ; Wegelin, 1926). The explanation for

this difference between the thyroid and other organs is to be found in its greater instability and readiness to enlarge in females, particularly between the ages of 10 and 20 years.

The enlargement at puberty does not usually lead to visible or clinical enlargement. In most cases the clinically enlarged glands of adolescence, belonging to Group (b), become less visible, or invisible, after puberty. Glands of Group (b), like those of Group (a), could therefore be regarded as within the limits of normal, unless it can be shown that they have a significantly higher incidence in goitrous areas, or in nutritionally and hygienically unfavoured social groups as compared with more favoured ones. We have no knowledge of the extent to which children and adolescents showing the Group (b) type of enlargement are rendered more liable than other children and adolescents to the development of established goitres in later life.

The glands of Group (c) are so conspicuous that it is reasonable to assume a hyperplasia which is outside physiological limits, whether or not they later return to normal. Even in this group, however, enlargement does not necessarily persist and we do not know in what proportion an established goitre follows in later life.

The time of appearance and disappearance of enlargement is of some importance. The earlier in childhood a gland becomes visible, and the longer it remains visible after the age of 17 or 18 years, the more likely is it that the gland will develop abnormally in response to an iodine insufficiency and that changes other than those of a physiological and transitory nature have occurred or will occur. A child of 9 or 10, or a young woman of 20, with a clinically enlarged gland, even though it be soft, smooth and symmetrical, could more reasonably be considered to show the early stages of a "goitre" than an adolescent of 14 to 17.

II.—ENDEMIC GOITRE IN GREAT BRITAIN IN RELATION TO THE IODINE, CALCIUM AND FLUORINE CONTENT OF THE WATER SUPPLY

BY

MARGARET M. MURRAY, J. A. RYLE, BEATRICE W. SIMPSON AND DAGMAR C. WILSON

Distribution of goitre and thyroid enlargement in Great Britain

A study of medical and scientific literature from 1800-1924 revealed that goitre had been looked for and recorded as endemic in parts of some 30 of the English counties and in certain regions of Wales (Iodine Facts, 1946). It appears to have been generally recognized that in Derbyshire, Gloucestershire, Nottinghamshire and Somersetshire there was a particularly high incidence and degree of severity.

In 1924 the Board of Education organized a survey of goitre incidence among school-children in most of the English and Welsh counties (Stocks, 1927 ; 1928). The findings showed a high incidence of goitre and thyroid enlargement among children in the 12-year-old age group in 17 out of the 39 English counties and in 5 out of the 10 Welsh counties surveyed.

Observations recorded since 1924 have confirmed and extended these earlier findings, and since 1943 the authors of this report have personally observed that in certain parts of 30 English counties and in the counties of South Wales goitre is still to be found, particularly in rural areas, without long searching. As a result of these latter observations it appears that to the list of counties named above for their high incidence Devonshire, Dorsetshire and Oxfordshire should be added.

For Scotland, the information is scanty. There are no statistics for the distribution of youthful thyroid enlargements comparable with those collected by the Board of Education in England. Goitre in Southern Scotland was formerly known as "Nithsdale Neck" from its high incidence in that Dumfriesshire valley (Mitchell, 1862). Records, including those made by the present authors, give evidence of goitre in 15 Scottish counties (Iodine Facts, 1946).

Data for Ireland are also scanty, but goitre has been reported from 6 counties of Eire (Macnamara, 1862 ; Martin 1862 ; Shee, 1940). Shee (1939 ; 1940) found "goitre" in 28 per cent. of 9,683 school-children under 14 years of age in the South Riding of County Tipperary, but in Galway City only one case was seen amongst 1,318 children. Examination of immigrants from Northern Ireland to the United States of America by Oleson and Neal (1930) showed a considerable incidence of simple goitre in persons coming from all six counties. Erskine (1933) considered goitre as endemic in South County Antrim, and our own observations on women from Northern Ireland, made on their arrival at English war factories, confirmed the occurrence of goitre previously recorded.

Changes in water supply effected by the substitution of large-scale undertakings for local wells are recognized as having lowered the incidence of goitre in some former endemic areas, for example in Derbyshire (Turton, 1927) and Somerset (Wilson, 1941). Occasionally a new provision of water has increased goitre incidence, as for instance after the introduction of a new supply of a very hard water into the Melton Mowbray district of Leicestershire (Turton, 1943). Increased incidence of goitre in parts of Montgomeryshire during the past 30 years has been ascribed to a new source of water supply taken off the moors (Joll, 1932). The late Dr. J. M. Martin, when County Medical Officer of Health, summarized (1936) the results of observations on endemic goitre in Gloucestershire extending over 25 years. He made a forecast of possible future alterations

in the distribution of thyroid enlargement in the Forest of Dean consequent on changes in the water supply. A visit to this district during the present enquiry confirmed Martin's observations as well as the earlier findings of Currie (1871). Residents formerly had recognized only certain of the Forest springs as sources of "whin" (goitre). The results of a goitre survey of women industrial workers from homes in the Forest of Dean (see p. 21) suggested no geographical localization of the goitre distribution, enlarged necks being recorded from all parts of the Forest. The Forest of Dean has now two main sources of water in general use, namely the East Dean supply, which drains coal measures, and the West Dean supply from the Old Red Sandstone.

Incidence of goitre and thyroid enlargement in relation to iodine content of water supply

For many centuries it has been a common belief in some parts of the world that the quality of the local drinking water may determine the incidence of goitre. The modern view that iodine deficiency in such drinking water plays an important part in causing endemic goitre seems to have been formulated in 1830, some 18 years after the discovery of iodine. This view was supported by the demonstration that iodine was abundantly present in burnt sponge, which for long had enjoyed a reputation for the treatment of goitre (Harington, 1933). The attempts by Chatin (1850) to prove that iodine deficiencies in water, soil and air were responsible for endemic goitre did not gain the immediate recognition which they deserved, and were not fully appreciated until the discovery that iodine was a normal constituent of the thyroid gland (Baumann, 1896).

Chatin's findings have since been confirmed in Switzerland (von Fellenberg, 1923), in different areas of the United States (McClendon, 1927) and in other parts of the world. The relationship between the iodine content of drinking waters and the incidence of goitre was clearly shown by McClendon and Williams (1923) from the records of the examination of American Army recruits. These authors established the fact that areas supplied by waters containing 3 μg. or more of iodine per litre were almost goitre-free.

Effects of Absolute or Relative Iodine Deficiency

Horsley (1886) showed that thyroidectomy in bitches before pregnancy was followed by the development of goitre in the offspring. Ten years later Halsted (1896) described very clearly the compensatory hypertrophy of the thyroid which follows the removal of a considerable part of the gland ; Marine and Lenhart (1909) demonstrated that administration of iodine could prevent this hyperplasia. Mellanby (1934), from the results of a series of controlled experiments on dogs, showed that the offspring of bitches kept under laboratory conditions and fed on a diet consisting of the common foodstuffs, milk, meat, bread and cabbage, developed large goitres of the parenchymatous hyperplastic type ; he further demonstrated that these glands could become normal in size and structure if a source of iodine, such as potassium iodide or cod liver oil, were administered directly after weaning. The natural occurrence of goitre in man and lower animals was studied by Marine (1928), who pointed out that the degree of thyroid hyperplasia in spontaneously occurring thyroid enlargement was inversely proportional to the iodine content of the gland. Among factors which might render insufficient an otherwise adequate intake of iodine, he included excess of fluorine in, and pollution of, the water supply, but he noted that in some goitrous regions waters were bacteriologically pure. Gross contamination of water such as occurs in some Indian endemic areas, to which the work of McCarrison (1928) drew particular attention, is probably a factor of minor importance in this country.

The accurate estimation of minute quantities of iodine is clearly an essential pre-requisite to any study of a possible causal relation between iodine deficiency and goitre. In this country the improved analytical procedure devised by Harvey (1935) enabled Young and his colleagues (Young *et al.*, 1936) to study the relation of the iodine contents of water, milk and pasture to the occurrence of endemic goitre in two English districts. One of these was situated in Somerset, where was found a very high incidence of goitre and an average of only 2·9 μg. iodine per litre in the drinking waters; the other district, in Suffolk, had a very low goitre incidence and an average iodine content of 8·2 μg. These workers considered that their results demonstrated once more the recognized connection between environmental deficiency of iodine and the incidence of endemic goitre, but suggested that the absolute iodine content of the soil might be less important than its mode of combination, which in turn might affect its availability. They also deduced from their observations that the difference in iodine content of the water in the two regions was not in itself sufficient to account for the difference in the goitre incidence, and suggested that there was either some other factor in the soil or water responsible for the high goitre incidence in Somerset, or that the availability of the iodine was different in the two places. It is to be noted that Somerset waters have iodine contents which are at the lower limits of those which McClendon and Williams (1923) found in goitre-free areas, but are also very hard. Since the iodine determinations which form the subject of this report were also made by Harvey's method, the present observations are comparable with those of Young and his colleagues.

In Stocks' (1928) analysis of the figures obtained in the 1924 Board of Education survey, he remarked that, excluding "goitre" areas, there remained for the "non goitre" areas a *residual* incidence rate for thyroid enlargement in children aged 12 years, which was one per cent. for boys and four per cent. for girls and this he regarded as a measure of normality. In our examination of children aged 11 to 15 years in three specially chosen areas—Okehampton, North Oxfordshire and Windsor—the lowest incidence of "visible" glands appeared to be of the order of 6 per cent., which corresponds fairly well with Stocks' "residual" rate. Our figure was higher than his, probably because children up to 15 years of age were included by us. This "residual" rate of 6 per cent. was found at Windsor, where the iodine content of the water (10·1 μg. per litre) is about ten times that recorded for Okehampton (1·1 μg. per litre), in which locality the incidence of "visible" glands was 26 per cent. (Table I). It is a question already raised by Shee (1939) whether any clinical enlargement should be regarded as within the physiological limits of normal, seeing that in regions of low incidence of adult goitre, and of high iodine-containing water, over 94 per cent. of the children show no such enlargement. Even in the Windsor area it is estimated that the daily intake of iodine from water, assuming a consumption of two litres per day from food and beverages, could not exceed 20 μg., which is only a small part of the estimated requirement.

After these three areas had been studied, a survey was made at Maldon, Essex, where the water has a very high iodine content. Here the incidence of visible glands was only 2·5 per cent. The high iodine content of Maldon water, taken in association with a generous intake of sea fish, probably makes such a locality fall into line with Iceland and Japan. Sigurjönsson (1940) has collected data concerning the size and condition of the thyroid gland in the inhabitants of Reykjavik, Iceland, where the iodine intake is probably much greater than anywhere else in the world except Japan, and has compared his figures with those obtained in other countries, goitrous and non-goitrous. His results show that in Iceland the gland is at all ages smaller yet richer in iodine

TABLE I

Incidence of Enlargement of the Thyroid Gland in Children, aged 11 to 15 years, from Four Areas with Drinking Waters Varying Greatly in Iodine Content

(Observers : J. A. Ryle, Margaret M. Murray and Dagmar C. Wilson)

Area	*Iodine content of water (μg. per litre)*	*Total hardness of water (as mg. $CaCO_3$ per 100 ml.)*	*No. of children examined*			*State of thyroid gland (see p. 9)*			*Total no. of visible thyroid glands observed (b, c and d)*	*Mean percentage incidence of visible thyroid glands (b, c and d)*			*Ratio of percentage incidence of thyroid glands visible in girls to that in boys (F/M)*
			Total	*Boys*	*Girls*	*Visible at rest (b)*	*"Rossetti" neck (c)*	*Pathological (d)*		*Total*	*Boys*	*Girls*	
Okehampton, Devon	1·1 (very low)	0·48 (soft)	298	153		27	1	2	30	26·2	20		1·7
					145	38	7	3	48			33	
North Oxfordshire	mean 2·0 (low)	mean 30·16 (hard)	451	188		21	2	6	29	18·0	15		1·3
					263	40	6	6	52			20	
Windsor, Berks.	10·1 (high)	31·65 (hard)	461	225		7	—	—	7	6·7	3		3·3
					236	21	—	3	24			10	
Maldon, Essex	50·2* (very high)	5·02 (soft)	527	220		2	—	—	2	2·5	1		4·0
					307	11	—	—	11			4	

* Wantz Road Well.

(calculated as iodine content per gram of fresh weight) than in other non-goitrous areas or countries. Shee (1940) questioned the validity of regarding the enlargement commonly seen in adolescent girls as a normal physiological response. It is conceivable that, with higher intakes of iodine, visible glands would become still rarer, in which case it might be agreed that the physiological limits of "normal" should not include glands which are visible.

It is worth noting that, as in the case of established goitre, the female-male ratio of thyroid enlargement falls and that the "Rossetti" necks are present in greater proportion where the total incidence of enlargement is high (Table I). The occurrence of pathological glands, that is to say of cases in which the gland besides being enlarged is firm or asymmetrical or nodular, would seem to be almost confined to areas in which the general incidence of enlargement is high and adult goitre has long been recognized as common.

Surveys undertaken to determine goitre incidence at all ages in rural populations are laborious and inconvenient (see p. 9), and only one village survey has been made during the course of this work. School-children at ages of 11-15, in which period of life the gland begins to become visible with significant frequency, provide the most accessible and convenient material for the study of thyroid enlargements. By employing elementary and secondary school populations of the same age, valid comparisons can be made between one area and another without recourse to surveys of the adult population, and the results can then be correlated with the iodine contents of local water supplies. The incidence of enlarged thyroid in childhood and adolescence has been found to be related to the incidence of adult goitre, and to vary significantly from areas of low to areas of high goitre endemicity (Stocks, 1928).

In the course of the present investigation about 4,000 school children were examined for thyroid enlargement by the method described on p. 7. The results of this survey, as well as those of the survey made for the Board of Education in 1924, confirm a high incidence of thyroid enlargement in children living in the English goitre belt. It should be remembered, however, that the data collected in 1924 were obtained not by a few trained individuals employing identical methods, but by about 600 school medical officers working independently ; the criteria of enlargement were not generally agreed upon or clearly defined, no distinction was attempted between the different types of enlargement, and the age of the children examined (12 years) did not include the whole period of adolescence nor the beginning of that period (14 to 17 years) in which enlargements are probably commonest.

Surveys on School-children

An opportunity arose to compare school populations using waters having a low iodine content with others using waters with a high iodine content.

Four areas, about which some information was already available, were chosen : (a) in and around Okehampton (N. Devon) with a soft water low in iodine (1·1 μg. per litre) ; (b) towns and villages in N. Oxfordshire with hard waters low in iodine (2·0 μg. per litre on the average) ; (c) Windsor (Berks.) with a hard water high in iodine (10·1 μg. per litre) ; and (d) Maldon (Essex) with a soft water exceptionally high in iodine (50·2 μg. per litre).

There were no other important social or nutritional differences between the four groups, in all of which, with the exception of the Maldon group, the consumption of sea fish may be presumed to have been low. The general nutrition was reasonably good considering the stringencies of wartime rationing. Evacuees were not included unless they had resided for three years or more in the locality under survey. The number of children examined in each

TABLE II

Thyroid Enlargement in Children, aged 11-17 years, in Selected Areas of England and Scotland in relation to the Mineral Content of the Water Supply

(Observers : J. A. Ryle, Margaret M. Murray and Dagmar C. Wilson, with Leonora Evans (Dorset), Agnes Turner (Dumfries) and A. M. Frazer (Inverness))

A. ENGLAND

County	*Town or area*	*Iodine content of water (μg. per litre)*	*Fluorine content of water (μg. per ml.)*	*Total hardness of water (as mg. $CaCO_3$ per 100 ml.)*	*Total calcium content of water (mg. per 100 ml.)*	*Total magnesium content of water (mg. per 100 ml.)*	*No. of children examined*			*Mean percentage incidence of visible thyroid glands (b, c and d)*		
							Total	*Boys*	*Girls*	*Total*	*Boys*	*Girls*
BERKS.	Windsor	10·1	0·15	31·65	12·2	0·28	461	225	236	7	3	10
DEVON	Okehampton	1·1	0·35	0·48	0·19	0	298	153	145	26	20	33
DORSET	Dorchester	3·1	0	23·27	8·85	0·28	151	—	151	24	—	24
	Sherborne	1·6	0	28·44	10·42	0·58	60	—	60	43	—	43
ESSEX	Maldon	50·2†	5·0	5·02	0·96	0·63	590	246	344	2	1	3
HERTS.	St. Albans	3·6	0·15	32·42	12·45	0·31	100	19	81	19	10	21
OXON.	Banbury	2·1	0·15	25·5	9·0	0·72	98	50	48	23	10	37
	Bicester	2·4	0·1	38·42	14·6	0·46	86	44	42	10	7	14
	Chipping Norton	1·8	0·2	27·53	10·6	0·25	163	65	98	19	14	22
	Finstock	2·3	0·18	29·80	10·92	0·60	108	38	70	19	11	23
	Hook Norton	1·7	0·15	39·15	13·98	1·01	72	29	43	35	31	37
	Witney	2·0	0·2	20·56	7·57	0·45	138	68	70	25	21	29

DUMFRIES	Annan Burgh	2·5	0·35	5·12	1·41	0·38	168	82	86	9	7	10
	Dumfries Burgh	2·0	0	2·60	0·79	0·15	216	94	122	17	12	20
	Gretna Township	1·8	0	3·75	0·99	0·30	93	54	39	9	4	18
	Kirkconnel	(New) 1·5 (Old) 1·8	0·1 0	1·06 5·75	0·24 1·75	0·11 0·35	53	17	36	19	23	17
	Langholm	1·6	0·05	12·56	2·96	1·24	138	70	68	20	20	21
	Lockerbie Burgh	2·0	0·1	8·25	2·47	0·5	52	31	21	23	16	33
	Moffat	1·6	0	4·15	1·12	0·33	100	52	48	9	8	10
	Morton Sch. and Wallace Hall	1·8	0	3·33	1·0	0·20	162	92	70	10	5	16
	Sanquhar	1·5	0·1	2·70	0·71	0·22	78	42	36	6	2	11
INVERNESS	Fort William	0·8	0·1	1·72	0·57	0·07	164	83	81	10	6	15
	Glen Urquhart	1·1	0·1	1·41	0·43	0·08	60	26	34	42	35	47
	Inverness Burgh	1·6	0·3	4·44	1·46	0·19	209	103	106	11	4	17
	Kingussie	0·8	0·1	1·70	0·46	0·12	93	40	53	17	3	28

† Wantz Road Well.

TABLE III

Relation of "Goitre" in Children to the Mineral Content of the Water Supply

(Board of Education Survey (1924) [see Stocks, 1928]: Waters analysed 1944-45, the supplies having remained unchanged)

A_1 "Goitre" incidence over 10 per cent.

County	*Town or area*	*Iodine content of water (μg. per litre)*	*Fluorine content of water (μg. per ml.)*	*Total hardness of water (as mg. $CaCO_3$ per 100 ml.)*	*Total calcium content of water (mg. per 100 ml.)*	*Total magnesium content of water (mg. per 100 ml.)*	*Mean percentage incidence of "goitre" among boys and girls in the 12 year old age group (Stocks, 1928)*
BUCKS.	Chepping Wycombe	4·4	0·2	29·02	9·8	1·10	15·72
CARMARTHEN	Carmarthen	2·0	0·2	1·25	0·24	0·16	18·07
CHESHIRE	Chester	1·2	0·3	5·75	1·70	0·36	15·80
	Congleton	2·9	0·1	28·50	7·55	2·31	12·15
	Crewe	3·0	0	11·05	3·6	0·51	11·78
	Hyde	1·3	0	3·45	0·88	0·30	11·21
	Stalybridge	1·8	0·15	4·46	1·23	0·33	15·44
DERBY	Ilkeston	2·4	0·35	10·97	1·95	1·46	16·94
DORSET	Poole	1·0	0·3	11·93	4·3	0·30	10·81
HEREFORD	Hereford	2·1	0·3	6·33	2·2	0·20	21·25

LANCS.	Preston	1·9	0·2	2·89	0·77	0·23	17·44
MONMOUTH	Ebbw Vale	1·0	0·3	0·55	0·22	Trace	31·36
NOTTINGHAM	Mansfield	2·0	0·5	15·95	3·55	1·71	14·09
SUFFOLK	Lowestoft	3·9	0·1	18·54	5·85	0·94	11·45
YORKSHIRE	Harrogate	1·3	0·6	5·61	1·64	0·38	11·28

B. "Goitre" incidence under 6 per cent. ("residual")

BEDS.	Luton	5·4	0·1	31·15	11·95	0·30	3·67
HANTS.	Southampton	3·8	0·15	28·97	11·10	0·28	2·05
	Newport, Isle of Wight	4·6	0·15	21·58	8·25	0·23	0·79
KENT	Margate	8·0	0·15	27·88	10·9	0·14	0·24
NORTHUMBER-LAND	Tynemouth	3·8	0·25	8·17	2·2	0·63	0·17
WILTS.	Salisbury	2·9	0·22	26·59	10·17	0·28	0·12
YORKSHIRE	Kingston-on-Hull	5·6	0·1	23·98	9·15	0·25	0·35

of the four areas was between 300 and 500. In all, 1,737 children aged 11 to 15 were examined.

The results given in Table I, p. 14, showed a high mean percentage incidence of enlargement and a low ratio for female/male incidence in the two areas with waters low in iodine. Windsor and Maldon, with waters of high iodine content, show only a low, "residual" rate of incidence and a high female/male ratio.

Twelve areas in all were surveyed in England, chosen mainly because goitre had been recorded therein previously, and thirteen in Scotland, chosen because the water iodine level was known to be low (see Table VI, p. 25). The results of these surveys are given in Table II which, incorporating some of the data in Table I, records the examination of 3,911 school-children aged 11 to 17 years and shows the mean percentage incidence of all thyroid glands visible at rest, including those with pathological changes.

A comparison of the incidence of "visible" glands (Table II) with the iodine level in the water is complicated by the fact that there were other disturbing factors to be taken into account, for instance the hardness of the waters, which is considered later (p. 26). It may be noted that in only two areas other than Windsor was a low "residual" (*i.e.*, 6 per cent. or under) incidence of "visible" glands found. One area was at Sanquhar, Dumfriesshire, where the water had a low iodine content but was soft ; the other area was at Maldon, Essex, where the water had a high iodine content.

To cover a larger field and to obtain further figures on which an estimate might be made of possible correlation between the incidence of thyroid enlargement in school-children and the mineral content of the water, additional areas were chosen from those surveyed for the Board of Education in 1924 and recorded by Stocks as having, respectively, a high incidence (over 10 per cent.) of enlarged glands, or a "residual" incidence (under 6 per cent.). The districts were chosen at random among those in which it was ascertained by personal enquiry that the water supply in use in 1924 had remained unchanged. In Table III, A and B, are given the results of this enquiry. It should be noted here that in areas with a high incidence of goitre (A) only three out of fifteen had waters with 3 μg. or more of iodine per litre, whereas in areas with only a "residual" goitre incidence (B) six of the seven areas had waters with more than 3 μg. of iodine per litre.

Survey of a Village Population

During this enquiry an opportunity arose of making a survey of a village population at Hook Norton, a remote North Oxfordshire village, which had at the last census (1937) a population of 1,153. It was possible to examine the condition of the thyroid in 575 inhabitants, of whom 218 were males and 357 females, and whose ages varied from 3 months to 70 years.

Enlargement of the thyroid was found in 149 persons. Among these were 35 in whom the enlarged gland was soft, smooth and symmetrical, and 114 with established goitre, in whom the gland was either hard, nodular or asymmetrical. The former type of enlargement had its maximum incidence in adolescence, while goitre was associated with adult life. Fig. 1 (p. 21) gives the percentage distribution according to age of the two types.

There are two sources of water supply in the parish. Both are hard waters with a mean total hardness of 34 degrees (see p. 27). Both have a low content of iodine, 1·5 μg. per litre (mean), and a mean fluorine content of 0·3 μg. per ml.

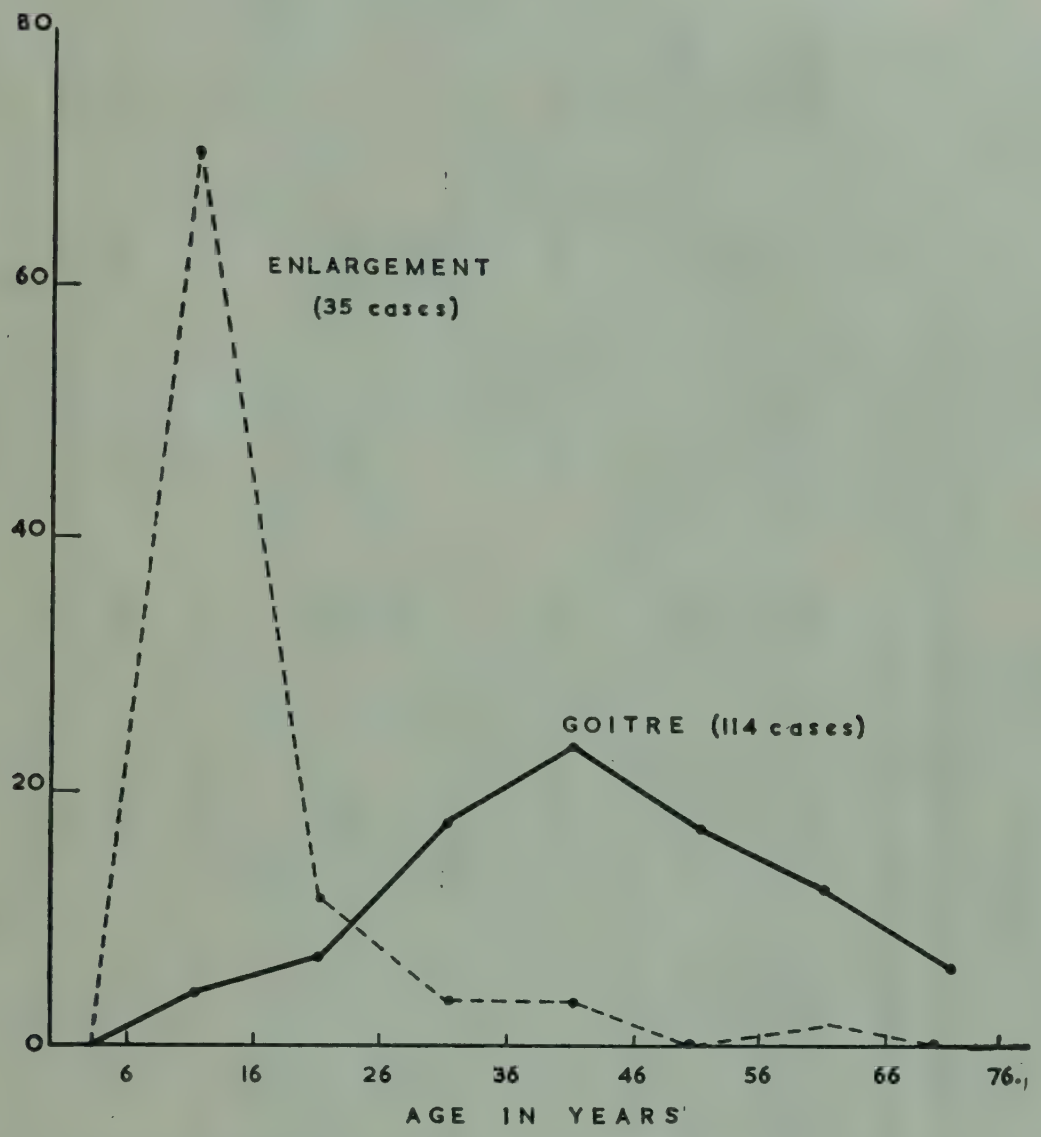

FIG 1. *Percentage Distribution, according to Age, of Thyroid Enlargement and Goitre in the Village of Hook Norton.

Surveys on Adult Women

During the examination of groups of women employed in war industries in Dorset, Gloucestershire and Oxfordshire, it was possible to study the incidence of thyroid enlargement in 1,780 women, aged 16 to 60 years, in relation to the mineral content of their water supply. The results are given in Table IV. The waters in the Dorsetshire and Oxfordshire areas had low iodine contents, but the high incidence of thyroid enlargement (48 per cent. of glands "visible at rest", including pathological types) recorded among women whose homes were in the Forest of Dean was associated with iodine contents which are not very low (2·6 to 3·1 μg. per litre). This, however, was a closed community of Forest people among whom there had been much intermarriage, and the present finding of a high goitre incidence in this district is in line with that recorded by previous observers.

* Fig. 1 is reproduced by courtesy of the Editor of the *Lancet* in which journal it appeared originally (Lancet, 1944, i, 107).

TABLE IV

Thyroid Enlargement in Women in relation to the Mineral Content of the Water Supply

(Observers : J. A. Ryle and Dagmar C. Wilson, with R. Wilson Carey (Brockworth))

County	*Town or area*	*Iodine content of water (μg. per litre)*	*Fluorine content of water (μg. per ml.)*	*Total hardness of water (as mg. $CaCO_3$ per 100 ml.)*	*Total calcium content of water (mg. per 100 ml.)*	*Total magnesium content of water (mg. per 100 ml.)*	*No. of women examined*	*Percentage incidence of visible thyroid glands (b, c and d)*
DORSET	Bridport Sherborne Weymouth	1·6	0	28·44	10·42	0·58	99	19
GLOS.	Brockworth	3·2	—	—	—	—	1,276	9
	Forest of Dean	2·6 3·1	0·2 0·2	38·9 23·2	6·93 6·29	5·2 1·8	50	48
OXON.	Chipping Norton	1·8	0·2	27·53	10·6	0·25	25	32
	Hook Norton	1·7	0·15	39·15	13·98	1·01	193	50
	Oxford	2·2	0	29·22	10·72	0·58	137	17

Discussion of Evidence relating Incidence of Thyroid Enlargement to Iodine Content of Water Supply

In Tables I, II, III and IV are given the results of the assessment of the state of the thyroid gland in the areas investigated, together with the results of the analyses of the drinking water. While it has generally been accepted, mainly because of the striking investigations of McClendon and Williams (1923) in the United States of America, that there is an inverse relation between the incidence of goitre and the iodine level in the water, such a clear-cut deduction cannot be made from the results of our investigations in the areas of Britain set out in Tables II and III. Nevertheless the results from the four areas contrasted in Table I, which were areas with very marked differences in iodine content, do bear out the general hypothesis. McClendon and Williams, as a result of data obtained from the routine examination of 2½ million United States recruits for the 1914-18 War, reported the following figures relating the goitre rate to the iodine content of representative river waters :—

Iodine in Water (*μg. per litre*)	*Goitre Rate* (*per thousand men*)
0 — 0·5	15 — 30
0·5 — 2	5 — 15
3 and above	0·1

It is to be noted that areas with 3 μg. or more of iodine per litre were practically goitre-free. Out of a list of 123 samples of U.S.A. drinking waters, 97 showed a value below 1 μg. per litre (McClendon, 1939). von Fellenberg (1933) found most Swiss waters very low in iodine, containing between 0·2 and 1·5 μg. per litre. By comparison, the waters of the areas studied in the present report were not very low in iodine (Tables V and VI). The facts that a considerable incidence of thyroid enlargement in children and goitre in adults can occur in places where the water contains 2 to 3 μg. of iodine per litre (Tables II and III), and that a high percentage of goitre exists in adults in an area such as the Forest of Dean (Table IV) where the iodine content of the waters ranges from 2·6 μg. per litre to 3·1 μg. per litre, suggested that in order to ensure against the occurrence of endemic goitre a higher level of iodine is required in this country than in the U.S.A. areas studied by McClendon and Williams. These deductions, taken in conjunction with, first, the absence of a clear-cut inverse relation between iodine in water and goitre for the areas included in Tables II and III, and, secondly, the generally lower incidence of thyroid enlargement in Scottish areas compared with areas in England with waters of similar iodine level (Table II), point to the involvement of other factors in the causation of endemic goitre. Such a hypothesis was put forward by Young *et al.* (1936) and formed the starting point of the present investigations. Although it was realized that the soil iodine content had been considered of equal importance with that of water in New Zealand (Hercus *et al.*, 1925), it was decided to investigate the possibility, often suggested by previous workers, that the degree of hardness of the water might also be a factor in the causation of endemic goitre.

If there is in the British Isles, as McClendon and Williams suggested there was in the United States, a "non-goitrous" level for the iodine content of drinking water, the present investigations suggest that this should be put at 5 μg. or more per litre for hard waters and possibly at 3 μg. per litre for soft waters.

Iodine content of some British waters in relation to geological formation.

Eighty-one samples of English and Welsh waters were analysed (Table V) after preliminary observations on goitre occurrence had been made. In the case of Scotland, the drinking waters from 64 towns were analysed (Table VI). Goitre surveys were made later in two counties—Dumfries and Inverness, in

which the water showed a relatively low iodine content. Of the 81 English waters, 40 had less than 3 μg. of iodine per litre, and of 64 Scottish waters, all but three were below 3 μg. per litre. That the incidence of goitre in Scotland was generally less than might be expected from the very low iodine content of the waters is possibly associated with the general softness of the Scottish water supplies.

TABLE V

Iodine Content* of 81 Samples of Water from England and Wales (including 8 from London)

Forty out of the eighty-one samples contained less than 3 μg. of iodine per litre.

No.	*County*	*Place*	*Iodine content of water (μg. per litre)*
1	Dorset	Poole	1·0
2	Derby	Derby	1·0
3	Monmouth	Ebbw Vale	1·0
4	Devon	Belstone	1·1
5	Devon	Okehampton	1·1
6	Glam.	Aberdare (Nantamen Fach.)	1·1
7	Glam.	Pontypridd	1·2
8	Cheshire	Chester	1·2
9	Cheshire	Hyde	1·3
10	Lancs.	Darwen (Sunnyhurst)	1·3
11	Yorkshire	Harrogate	1·3
12	Oxon.	Hook Norton (Down End Tite)	1·4
13	Warwick	Nuneaton	1·5
14	Glam.	Aberdare (Pwllfa)	1·5
15	Dorset	Sherborne	1·6
16	Durham	Westgate	1·6
17	Oxon.	Hook Norton (Down Town Tite)	1·7
18	Lancs.	Darwen (Earnsdale)	1·7
19	Cheshire	Stalybridge	1·8
20	Oxon.	Chipping Norton	1·8
21	Lancs.	Preston	1·9
22	Yorkshire	Mansfield	2·0
23	Lancs.	Darwen (Bolton supply)	2·0
24	Carmarthen	Carmarthen	2·0
25	Oxon.	Witney	2·0
26	Yorkshire	Wakefield	2·0
27	Oxon.	Banbury	2·1
28	Hereford	Hereford	2·1
29	Oxon.	Swerford	2·2
30	Devon	Taw River	2·3
31	Cheshire	Wallasey (Alwen supply)	2·3
32	Oxon.	Finstock (Fawler spring)	2·3
33	Denbigh	Wrexham	2·4
34	Derby	Ilkeston	2·4
35	Oxon.	Bicester	2·4
36	Devon	West Okement River	2·4
37	Glos.	West Dean Supply	2·6
38	Glam.	Aberdare (Nanty-moel Reservoir)	2·7
39	Cheshire	Congleton	2·9
40	Wilts.	Salisbury	2·9
41	Cambridge	Cambridge	3·0
42	Cheshire	Crewe	3·0
43	Oxon.	Tadmarton	3·0
44	Glos.	East Dean Supply	3·1
45	Dorset	Dorchester	3·1
46	Dorset	Crewkerne	3·2
47	Kent	S.W. Kent (Cranbrook Water Co.)	3·3
48	Hants.	Winchester	3·4
49	Durham	W. Hartlepool	3·4
50	Herts.	St. Albans	3·6
51	Staffs.	Wolverhampton (Cosford waterworks)	3·7
52	Hants.	Southampton	3·8
53	Northumberland	Tynemouth	3·8
54	Oxon.	Cowley Marsh (Crescent Road Well)	3·9
55	Suffolk	Lowestoft	3·9
56	Oxon.	Finstock (draw-well)	4·1
57	Hants.	Alresford	4·2
58	Bucks.	Chepping Wycombe	4·4
59	Wilts.	Swindon (Ogbourne St. George)	4·5
60	Staffs.	Wolverhampton (Tattenhall waterworks)	4·6
61	Hants.	Newport, Isle of Wight	4·6
62	Beds.	Luton	5·4
63	Yorkshire	Kingston-on-Hull	5·6
64	Berks.	Maidenhead	6·0
65	Hunts.	Huntingdon	7·1
66	Kent	Margate	8·0
67	Essex	Southend	8·2
68	Essex	Chelmsford	8·2
69	Cheshire	Wallasey (artesian bore)	9·0
70	Berks.	Tangier Island (shallow well)	10·1
71	Essex	Maldon (Spital Road well)	13·3
72	Essex	Maldon (Wantz Road source, 300 feet)	50·2
73	Berks.	Windsor (Ded-worth deep well)	52·2
		LONDON SAMPLES	
74		New River	5·1
75		Alma Road Well	7·5
76		Hoe Lane Well	7·9
77		Lee Bridge	8·4
78		Kempton Park	8·8
79		Hadley Road Well	11·1
80		East Ham	13·0
81		Old Ford Road Well	24·7

* *All estimations were made on 1 litre in duplicate, by the method of Harvey (1935).*

Table VI

Iodine Content* of 64 Samples of Water from Scotland

Sixty-one of the sixty-four samples contained less than 3 μg. of iodine per litre.

No.	County	Place	Iodine content of water (μg. per litre)
1	Perth	Blair Atholl	0·7
2	Forfar	Arbroath	0·7
3	Inverness	Fort William	0·8
4	Inverness	Kingussie	0·8
5	Peebles	Peebles	0·8
6	Wigtown	Wigtown	0·9
7	Aberdeen	Balmoral Castle	0·9
8	Aberdeen	Aberdeen (Victoria Park well)	0·9
9	Perth	Perth	0·9
10	Perth	Crieff	1·0
11	Aberdeen	Aberdeen (main supply)	1·0
12	Argyll	Inverary	1·0
13	Aberdeen	Ballater	1·1
14	Ayrshire	Dalmellington	1·1
15	Midlothian	Edinburgh	1·1
16	Inverness	Glen Urquhart	1·1
17	Renfrew	Greenock	1·1
18	Selkirk	Selkirk	1·2
19	Inverness	Portree, Skye	1·2
20	Island of Lewis	Stornoway	1·3
21	Ross and Cromarty	Ullapool	1·3
22	Ayrshire	Kilmarnock	1·3
23	Fife	Dunfermline	1·4
24	Fife	Elie	1·4
25	Lanark	Hamilton	1·4
26	Dumfries	Kirkconnell (New Supply)	1·5
27	Dumfries	Sanquhar	1·5
28	Lanark	Glasgow (Lock Katrine)	1·5
29	Dumfries	Moffat	1·6
30	Ross and Cromarty	Dingwall	1·6
31	Inverness	Inverness	1·6
32	Aberdeen	Newmachar	1·6
33	Shetland Is.	Lerwick	1·6
34	Dumfries	Langholm	1·6
35	Dumfries	Kirkconnell (old supply)	1·8
36	Fife	Kirkcaldy	1·8
37	E. Lothian	Haddington	1·8
38	Dumfries	Gretna (Winterthorpe)	1·8
39	Sutherland	Lairg	1·8
40	Banffshire	Banff	1·8
41	Kirkcudbright	Kirkcudbright	1·8
42	Dumfries	Morton (Lower Nithsdale and Mid-Annandale)	1·8
43	Morayshire	Elgin	1·9
44	Dumfries	Lockerbie	2·0
45	Aberdeen	Kingseat	2·0
46	Dumfries	Dumfries	2·0
47	Lanark	Glasgow (Gorbals)	2·1
48	Renfrew	Paisley	2·1
49	Kincardine	St. Cyrus	2·3
50	Kincardine	Bent Farm	2·3
51	Aberdeen	Turriff	2·3
52	Caithness	Wick	2·4
53	Sutherland	Dornoch	2·4
54	Argyll	Bunessan	2·5
55	Dumfries	Annan	2·5
56	Aberdeen	Peterhead	2·5
57	Bute	Rothesay (Ascog Loch)	2·5
58	Roxburgh	Jedburgh	2·6
59	Forfar	Brechin	2·6
60	Caithness	Thurso	2·6
61	Orkney Is.	Kirkwall	2·8
62	Bute	Rothesay (Dhu Loch)	3·6
63	Fife	Crail	5·0
64	Argyll	Oban	5·2

* *All estimations were made on 1 litre in duplicate, by the method of Harvey (1935).*

The distribution of thyroid enlargements in the areas covered in the present survey in relation to geological formation, which was summarized for us by Mr. C. N. Bromehead of the Geological Survey, agrees closely with that found by Stocks (1928) and earlier observers (Roberts, 1882; Berry, 1901). Places situated on the Old Red Sandstone, the Carboniferous Limestone, the Liasand Oolite divisions of the Jurassic and some parts of the Lower Cretaceous, h ave a significantly high incidence of goitre. Places on the older stratified formations show for the most part a low incidence except those where igneous intrusions occur. Most of the districts situated on later geological formations have a low incidence.

The suggestion that goitre is absent from districts near the sea is negatived by the distribution of endemic goitre in New Zealand. In the coastal district

of Christchurch there was in 1925 a high incidence of goitre and no demonstrable iodine in the deep well water (Hercus *et. al.*, 1925). In South Wales, a high endemicity of goitre along the Glamorgan coast has been reported by Davies and Rogers (1940).

Abnormally High Iodine Content of Certain Waters

In the present study, waters from certain deep wells were discovered to have an unusually high iodine content. These were the Wantz Road supply at Maldon, Essex, and the Dedworth supply at Windsor, Berks., which contained 50·2 and 52·2 μg. of iodine per litre respectively. These amounts are far above those present in sea water ; for instance, the average value for four samples collected from the sea at different places round the British Isles was 20 μg. per litre. The explanation of the high iodine content of Maldon and Windsor waters may possibly be connected with the recent discovery by Dr. K. P. Oakley of unidentified fossils rich in iodine still retaining organic material and preserved in peaty layers in Eocene and later sands in Hampshire and Norfolk. Two samples of such fossils from geographical formations comparable to those occurring at Maldon and Windsor were kindly supplied by him ; they weighed 2 mg. and 0·2 mg. respectively and, though too small to give an accurate result on a dry weight basis, were found to contain 0·02 and 0·1 per cent. of iodine respectively. It is possible that these organisms, or some similar fossil forms, may be responsible for the high iodine content of the waters at places such as Maldon and Windsor.

Iodine intake and absorption in relation to calcium and fluorine

(With the assistance of Josephine Stack, B.Sc.)

Calcium Content and Hardness of Water

Although from earliest times water has been considered a "cause" of goitre diverse explanations for the phenomenon have been put forward. Pollution can be ruled out in all the present investigations. The association of goitre with low iodine content of water has been dealt with above. The contributory factor cited as next in importance is hardness, or calcium and magnesium content. As long ago as 1769 Prosser in this country recognized that "Derby neck" was associated with the hard water of limestone regions, and many others have since discussed this point, including Berry (1901), von Fellenberg (1924) and McClendon and Williams (1922-23). According to Marine (1935), though calcium has been considered an aetiological factor in the production of endemic, or simple, goitre for more than a century, specific investigations of this point have yielded doubtful results. von Fellenberg (1924) pointed out that iodine tends to be leached out of soil rich in the carbonates of the alkaline earths, so that hard waters would tend to be low in iodine. It was already known (Marine, 1924), and the present investigations have confirmed the fact, that endemic goitre can occur in places with very soft waters, as for example in the counties of Inverness and Dumfries and in parts of N. Devon (see Table II, pp. 16 & 17). Moreover, von Fellenberg's hypothesis does not hold for places such as Windsor, where the water is hard but has a high iodine content, or Huntingdon, where the water is very hard and the iodine content high. Clearly calcium content, or hardness, of water must be regarded only as a contributory cause, and it must be considered in relation to other factors such as the iodine content.

Many investigators have designed experiments to elucidate the relation of calcium intake to the state of the thyroid in laboratory animals (see Cameron, 1945). Thompson (1933) showed that 67 per cent. of rats consuming diets low in both iodine and calcium developed some degree of reactive hyperplasia of

the gland. When the calcium content of the diet was increased, 100 per cent. showed hyperplasia, which was severe in 57 per cent. An adequate iodine intake prevented the hyperplasia on the high calcium diets. Thompson showed later (1936) that, when the calcium level of the diet was increased and the iodine level kept constant, the blood iodine was lowered ; this suggested either less absorption or greater excretion of iodine. Preliminary experiments by Simpson (1947) on iodine balance in rats have indicated that on low iodine diets, when the calcium content of the diet is increased, there is an increased iodine excretion and a fall in the iodine content of the thyroid. Marine (1935) stated in a review that experimental work abundantly confirmed the conclusion that excessive calcium intake in some manner increases the goitre-producing effect of any given diet. Goitre produced in rabbits by giving an excess of cabbage in the diet is an exception to this hypothesis.

In the present study, the waters of all areas surveyed for the incidence of thyroid enlargement have been analysed for mineral content. Analyses have also been made of the waters of many places included in the 1924 Board of Education survey where the sources of water have remained unaltered. These included fifteen localities with a high incidence and seven with a low or "residual" incidence of thyroid enlargement in children.

Determinations were made of the content of iodine, fluorine, total calcium and total magnesium ; from the last two figures, total hardness was calculated and expressed as mg. of $CaCO_3$ per 100 ml. of water. According to Suckling (1944) waters with less than 5 degrees of hardness (5 mg. $CaCO_3$ per 100 ml., where one degree of hardness = one part of hardness, calculated as $CaCO_3$, per 100,000 parts of water) are classed as soft, those with over 10 degrees of hardness (10 mg. $CaCO_3$ per 100 ml.) as hard and those with over 30 degrees of hardness (30 mg. $CaCO_3$ per 100 ml.) as very hard. It will be seen from the Tables that most of the English waters analysed were hard, whereas most of the Scottish waters analysed were soft.

In Tables I, II, III and IV are data concerning the iodine content of waters in relation to thyroid enlargement and goitre incidence, in addition to the calcium and magnesium content and the degree of hardness. The majority of the areas listed in Table II may be classified into : (a) those with soft waters, possessing under 5 degrees of hardness, and (b) those with hard waters, possessing over 20 degrees of hardness. For these two groups calculations of the means of the iodine contents, total hardness and percentage incidence of visible glands among children examined are given in Table VII. It will be seen that in spite of the higher mean iodine content of the hard waters there is a considerably greater incidence of visible glands in the areas with hard waters. Windsor, Maldon and Glen Urquhart are excluded from this calculation.

Fluorine Content of Water

Maumené (1866) expressed the view that excess of fluorine in drinking water might be the cause of endemic goitre, and Marine (1924) included fluorine as a possible contributory factor. From several parts of the world there have been reports of the co-existence of fluorosis and endemic goitre. Steyn (1938) recorded a large number of goitres in adults and children in parts of the North West Cape Province of South Africa, where fluorine occurs in the underground water. Wilson (1941) reported a high degree of dental fluorosis in the goitrous area of the Punjab, India, and the rocks of that region showed the presence of sufficient fluorine to account for the fluorosis. In Somerset, Wilson (1941) also found a certain parallelism between the incidence of goitre and dental fluorosis. In one region of North Oxfordshire where fluorine-bearing clays are found (Bromehead *et al.*, 1943), the co-existence of dental fluorosis and endemic goitre was established. von Fellenberg (1938) investigated the iodine

TABLE VII

Thyroid Enlargement in Children in relation to Hardness of Water : Calculated from Data given in Table II. (pp. 16 & 17)

No. of areas from Table II	*Mean total hardness of water (as mg. $CaCO_3$ per 100 ml.)*	*Mean iodine content of water (μg. per litre)*	*No. of children examined*			*Mean percentage incidence of visible thyroid glands (b, c and d)*		
			Total	*Boys*	*Girls*	*Total*	*Boys*	*Girls*
10	2·59 (soft)	1·5	1,466	730	736	13·4	8·7	18·5
9	29·45 (hard)	2·3	976	313	663	24	14·9	27·8

and fluorine content of water in relation to endemic goitre and found that low incidence of goitre was always associated with high iodine, but high incidence of goitre could occur in high or low fluorine areas. One explanation might be that while low iodine is the primary cause of endemic goitre, the apatites, which are forms of calcium phosphate, are often fluorine-bearing rocks and are usually poor in iodine. The problem of the association of goitre with fluorosis is therefore complex. In Iceland, where fluorosis is present but endemic goitre absent, the consumption of sea fish is very high (Sigurjönsson, 1940).

During the present goitre surveys an attempt has been made to test a possible association between endemic goitre and fluorosis by determining the fluorine content of the waters in all areas surveyed. Many English waters contain a small amount of fluorine, under one part per million, but only a few contain much more than this (Bromehead *et al.*, 1943). Mild degrees of dental fluorosis, however, occur in many localities (Spira, 1942 ; Bromehead *et al.*, 1943 ; Weaver, 1944). At Maldon, Essex, and neighbouring places, the waters contain up to five parts per million (5 μg. per ml.) and at a level as high as this any association existing between fluorosis and goitre ought to be apparent. The water at Maldon, however, is unusually rich in iodine, and this, together with the fact that much fish is eaten there, may ensure a large enough intake of iodine to outweigh any possible adverse effects of fluorine. Endemic goitre has not been reported from the fluorosis areas of the United States of America.

A profitable study of the relation of fluorine to endemic goitre could be made only in places where the waters have a relatively low iodine level. Suitable districts would be areas of India, China or North Africa or Italy where severe fluorosis and high goitre incidence have been reported to co-exist.

Environmental and hereditary factors influencing the iodine requirement

Iodine Requirement of Man

There is not at present enough evidence on which to make any satisfactory estimate of the human daily requirement of iodine. Only balance experiments carried out over long periods, or others involving the use of a radio-active isotope of iodine, could settle this point. Many workers have suggested values for man's requirement based in part on figures for iodine excretion and in part on deductions from animal experiments. The adult daily requirement has been variously given as 100 μg. (von Fellenberg, 1923), 50 μg. minimum and 150 μg. adequate (Lunde, 1929), 60-120 μg. (Remington *et al.*, 1936) and 20-40 μg. per 1,000 Calories or a total of 60-120 μg. (Orr and Leitch, 1929). It is recognized that for the purposes of prophylaxis iodine may be given in suitable doses at considerable intervals, because it can be stored in the thyroid.

If 100 μg. daily be taken as adequate for an adult, it would seem reasonable to assume that a larger amount, say 150 μg., is needed to meet the growth requirements of a child, an adolescent or a pregnant woman. If these assumptions are justified it has to be admitted that even in places where the water is rich in iodine it cannot supply more than a part of the requirement. Only two waters among the many analysed, namely, those at Windsor, Berks. (Dedworth deep well), and at Maldon, Essex (Wantz Road well), where the content is about 50 μg. per litre, would give as high an intake of iodine as 100 μg. on the basis of a daily consumption of 2 litres water (Magee, 1937). In most places the corresponding value would be less than 10 μg. daily. Water cannot therefore generally be the chief source of dietary iodine, although from the results of previous surveys as well as the present one, the iodine content of water would seem to be a factor determining the appearance of thyroid enlargement. In any case there must exist over wide areas a state of minimal intake which may easily become subminimal.

In some countries and districts foods rich in iodine may afford the main protection against the development of goitre. With a change of food habits this protection may vanish and goitre may increase in frequency. There was some evidence of a rise in the incidence of simple goitre in England towards the end of the 1914-18 War (Eason, 1939), which may have been partly due to the failure of the fish supply, a contingency prevailing at all times in more remote inland villages. It is already recognized that the second world war has resulted in an increased incidence of endemic goitre in China among the indigenous population of Yunnan Province (Robertson, 1941). Following the Japanese occupation of the Burma Road, the supply of sea salt was cut off, necessitating the use of local mines with a salt low in iodine content. Six months sufficed for the production of goitre in susceptible individuals among refugees to this area.

Soil iodine is also important. Sea fish, and products obtained from them such as cod liver oil, are the only common articles of diet which are good sources of iodine. In the course of the present work a few samples of common sea fish were analysed with the following results :—herring 220 μg. iodine, cod 312 μg., haddock 932 μg. per 100 g. dry weight. Assuming that 80 per cent. of the fresh weight is due to water, 100 g. (3½ oz.) portions of each of these fish would yield 44, 62 and 186 μg. of iodine respectively.

Cod liver oil and possibly other fish liver oils are among the few natural foodstuffs rich in iodine, and they form a possible iodine supplement for children. McClendon (1939) gives values for refined cod liver oil varying from 5,100 to 14,940 μg. per kg. A sample of the Ministry of Health's cod liver oil compound was found to contain 23,000 μg. per kg. If this can be taken as typical, then a child consuming a large teaspoonful, *i.e.* 5 ml., would thereby obtain approximately 100 μg. of iodine, which is a large part of the postulated daily requirement of 150 μg.

Goitre and Dietary Iodine from Sources Other than Water

It has already been noted that endemic goitre may occur in coastal districts. In such cases the local water supply is generally found to be low in iodine and fish is to be obtained only with difficulty or as a luxury which is not included in the customary diet. Thus in Dumfriesshire local salmon are sent to London markets, while in Glamorganshire and parts of Cornwall the conformation of the coast line does not permit of easy access to local fishing vessels. Occasionally local seaweeds are utilized, for example the "laver bread" on sale in Glamorgan markets, which contains 0·011 per cent. of iodine (11,000 μg. per 100 g.) when dried.

The high cost of fish, and its scarcity under war conditions, have been factors limiting its general use. In some rural districts fresh sea fish has never been on sale. In the present survey it was found that people who were unaccustomed to eating fresh fish did not willingly spend their ration points on tinned fish. In Hook Norton parish (Oxon.), for example, where there is no retailer of fresh fish, visits to the local shops elicited the information that less than 2d. per head monthly was expended on tinned fish. Results of an enquiry as to why fish was not more often included in the school meals provided by local authorities showed cost to be the determining factor ; when provided, fish was a popular item.

During the period of this survey wartime restrictions on fishing and the dispatch of fish to other parts of the country had lessened the supply of fish in North Scotland. Diminishing consumption of fish, lack of home-grown vegetables and widespread winter shortage of milk are among the unsatisfactory features of the diet in North Scotland discussed by Cathcart and his colleagues (1940). Sydenstricker (1944) found that many children in Scotland showed evidence of former rickets.

Investigations made during the present enquiry in Dumfriesshire and Invernesshire, showed that local traditions of thrift and self-respect prevented full use being made of the available school milk and meals. When two areas of the county of Inverness were compared, one inland and the other coastal, a marked difference was found in the incidence of thyroid enlargement, which was 25·8 per cent. among the inland school-children and 9·8 per cent. in the coastal area where fish was available. This difference was not due to a different age and sex distribution in the two groups, for statistical analysis showed that, if the goitre incidence among the children in the inland area had been the same as that found for the coastal children of the same age and sex, the number of expected cases would have been only 14·75, whereas in fact the observed cases numbered 41. As the difference between the actual and expected number exceeds six times its standard error, it is extremely unlikely to be a chance fluctuation. These data indicate a definitely increased incidence of thyroid enlargement among school-children in the inland areas of Inverness as compared with the coastal belt. All Invernesshire waters have a very low iodine content.

In Dumfriesshire little is now heard about the "Nithsdale neck". Economic conditions have changed in the Nith Valley since Mitchell (1862) observed goitre at Sanquhar and Thornhill. Weaving, a poorly paid industry, has been superseded by coal and lead mining, and there are now improved rail communications. Nevertheless, at the present time women with enlarged necks are seen in the less prosperous and more isolated agricultural parts of Annandale and Eskdale, and also in the poorer areas of Dumfries town.

Other Factors Determining the Occurrence of Adolescent Thyroid Enlargement or Adult Goitre

The fact that in no school visited in the course of this survey did the majority of the children show thyroid enlargement, and that in no village in an endemic area in this country do the majority of the population develop goitre, might be interpreted as indicating that a more pronounced degree of iodine deficiency is in fact required to produce thyroid enlargement than we have assumed. It might be argued that most people can adapt themselves to a sub-optimal intake without sustaining any harm, or that a proportion of the population are predisposed by inheritance or by environmental or nutritional disadvantages to the development of thyroid hyperplasia or goitre in the presence of a rather low intake of iodine. There is something to be said for each of these assumptions, but arguments in favour of the genetic factor can most reasonably be advanced. Thus it is common to find a family or families in a village in an endemic area in which goitre affects several members concurrently or several successive generations, notwithstanding the fact that neighbouring families of comparable social and economic status, drawing their water from the same sources, can record no case. Three illustrative examples may be cited.

Finstock, one of the North Oxfordshire centres of the cottage glove industry, is situated on the borders of Wychwood Forest. The inhabitants depend entirely on local springs and wells and use a hard water low in iodine (see Table II). The village is cut off from main roads by the rivers Evenlode and Windrush, and has no regular supply of fish. The men have usually gone out of the district to work and until the present war the women normally remained at home. The representatives of one Finstock family had themselves recognized goitre in 18 female and 2 male members. Though other cases of goitre were noted in this district, neighbours of many years' standing who had lived under apparently identical conditions showed no thyroid enlargement.

In Hook Norton, another agricultural parish in North Oxfordshire and until recently in an isolated situation, endemic goitre is recognized by the community as associated with certain families long identified with the village. A kinship group had marked goitre in 10 females and 2 males, one of whom, aged 52, was unable to wear an 18-inch collar. One girl, aged 12, belong-

ing to this family group had a "Rossetti neck" (gland "visible +"); she lived under very favourable social and economic conditions, but had always used a hard water of low iodine content (see Table II).

In Okehampton, Devon, the female members of a family, which for long had been resident in the district and for many years had used the town supply of soft water very low in iodine (see Table I), were locally distinguished from their neighbours by their large necks. The mother, aged 61, with a large cystic and nodular goitre and with auricular fibrillation, recalled that both her mother and grandmother had belonged to Okehampton and had developed goitres. Of her eight children now alive, four females on examination showed various degrees of thyroid abnormality; the fifth daughter, married and living away from home, had also some degree of thyroid enlargement; of the three sons, two were on active service, the third was found on examination to have a normal thyroid.

In respect of inherited or constitutional liability, goitre may, in brief, be considered as falling into line with other diseases of a chronic nature which are caused by the prolonged action of adverse factors. At the two ends of the scale we recognize respectively a high inborn liability, and a high resistance, to the development of the disease in persons exposed to an adverse stimulus of, say, quantity x and duration of exposure y. If either factor x or factor y is increased, a proportion of those with an intermediate degree of liability (or resistance) will develop the disease, but the increase may need to be considerable before cases appear among the more resistant group. If, on the other hand, x or y (or both) can be reduced, the disease may cease to appear even among those with the highest inborn liability. A comparable problem is the gouty diathesis which is still present in certain families and may occasionally lead to the development of the disease in persons living the most carefully regulated lives. In earlier days of gross over-eating and high alcoholic consumption the disease was prevalent.

In countries and among populations in which general nutritional standards are low, the iodine in drinking water is inadequate and sea fish are not obtainable, the incidence of goitre and cretinism is high, as for example in the Himalayan valleys of India, where these conditions might well appear in individuals who would not develop them in England. If, under the more favourable conditions obtaining in England, the iodine intake were raised to an optimal level by the universal distribution of iodized salt, it might be expected that goitre would eventually disappear even in the areas of present high endemicity. Sporadic cases also would become rarer, and only be recorded in persons with a very high susceptibility or an inability to make use of the available iodine.

Other effects of iodine deficiency

Cretinism

Gardiner-Hill (1934) has pointed out the risk of cretinism appearing in the later generations of goitrous families who continue to live in endemic goitrous areas, and the importance of investigating the occurrence of hypothyroidism in the mothers of "sporadic" cretins. During the present survey, records were obtained of cretins in Dorset, Gloucestershire, Oxfordshire and Wiltshire, and two families containing cretins were investigated.

In Swerford, adjacent to Hook Norton, and with the same source of water, a family of low-grade agricultural workers was visited. The mother and daughter were goitrous and two sons aged 38 and 32 were typical cretins of small stature and low mentality. These men lived at home and were able to do field work under supervision. Since adolescence they had occasionally been given thyroid medication. The second family lived in Cowley, Oxford, and included a male cretin aged 63 and a female cretin aged 61, both mentally sub-normal and requiring care in a Public Institution. They belonged to Oxford City, having always lived on Cowley Marsh. The family had numbered

13 when the father's earnings were only £1 weekly. Both parents, according to a photograph, had been well developed ; the mother's step-sister, still alive, had a large goitre. The son and daughter, who were cretins, had not received any thyroid medication until after adolescence. Two younger daughters were early recognized as having goitre and received thyroid treatment. They are now intelligent housewives ; one has a daughter with a "Rossetti neck" ("visible +"), who is the mother of a healthy infant. Until the provision of the Oxford City supply, water was obtained from a local well which has now been filled in.

Deaf-mutism

The association of congenital deafness with endemic goitre and cretinism was pointed out by Bircher (1883) and later by Nager (1926). Wespi (1945) noted the unusually high incidence of congenital deaf-mutism in Switzerland as compared with other European countries or the United States. In 1930 the incidence for Switzerland was 17·9 per 10,000 inhabitants ; the corresponding figure for France was 4·7. During the clinical investigations of the distribution of thyroid enlargement, Murray and Wilson (1945) noted that a relatively high incidence of deaf-mutism was found in districts where endemic goitre was prevalent and cretinism existed. In contrast with the state of affairs relating to goitre, men are affected with congenital deafness as often as women. In some cases, deaf-mutes show enlargement of the thyroid gland, in others there is a history of goitre in some other member of the same family. In three districts of Oxfordshire, namely Banbury, Chipping Norton and Woodstock, which comprise one area, there is endemic goitre, the water supplies are low in iodine (1·4 - 3·0 μg. per litre) and 28 deaf-mutes have been recorded in a total population of 36,653. In three districts of another area, Henley and Goring in Oxfordshire and Windsor in Berkshire, where endemic goitre is not prevalent and the iodine content of the waters is moderate to high (10 - 52·2 μg. per litre) 5 cases of deaf-mutism were present in a population of 38,910. (This comparison is based on the results of personal enquiries about the place of birth, age and residence of deaf-mutes made for us by the Rev. H. M. Ainger working for the Diocesan Association for the Deaf and Dumb, who also introduced us to these people.)

III.—GOITRE PROPHYLAXIS BY THE USE OF IODIZED SALT

BY

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It is agreed that the use of iodized salt is the most effective means of preventing simple goitre and other pathological conditions associated with a low iodine intake (Cameron, 1945). Large-scale prophylaxis in various parts of the world, including Switzerland, Poland and the United States, has proved the efficacy of its administration (Marine, 1928; Means, 1937). The consumption of the salt has in most cases been voluntary and encouraged by educational campaigns. In Poland, where there was a Government monopoly in salt, the whole supply to certain provinces was iodized.

Kimball (1938), from a study of the results of 20 years of prophylaxis in Ohio, U.S.A., claimed that not only was endemic goitre prevented, but at the same time cretinism, deaf-mutism associated with endemic goitre, and much sub-normal development in girls were also prevented. As the result of his long experience he added the warning that the iodine content of salt supplied for the prevention of endemic goitre should be checked yearly by some competent authority. In countries where unrefined salt, having a high content of iodine, is obtainable, the possibility of its use in preference to other sources of salt with low iodine content should be seriously considered (Kimball, 1946).

Experience in New Zealand has suggested that where iodine is used prophylactically, the dosage must be reviewed together with varying local factors, such as an increase in calcium intake, which may influence the availability of the iodine (Shore and Andrew, 1934). The Director General of Health for New Zealand in his Report for 1945 recorded a fall in the incidence of goitre in school-children from 20 per cent. in 1920 to 9·7 per cent. in 1940, as a result of the introduction and use of iodized salt.

The use of iodized salt over a period of 15 years (1922-37) in Appenzell, Switzerland, was followed not only by a decrease in goitre, but also by a lessened incidence of cretinism and deaf-mutism (Eggenberger and Messerli, 1938). Wespi (1945) has recorded evidence of a striking decrease of deaf-mutism in all cantons following the introduction of iodized salt. The decrease in each canton corresponded with the degree of adoption of iodized salt by the population.

Guided by the combined experience of other countries, the Goitre Sub-Committee of the Accessory Food Factors Committee (1944) considered that for Great Britain a salt containing 1 part of potassium iodide in 100,000 parts of sodium chloride should be both convenient and effective. With an average daily intake of 10 g. of salt per head, this would provide 0·1 mg. of iodide, or 76 μg. of iodine, per head daily. If packeted table salt only is iodized, then, since the estimated average intake of this is less than 3 g. per day, the level of iodization should be raised to an average of 1 part of potassium iodide in 40,000 parts of salt, the permitted limits of variation being between 1 part in 30,000 and 1 part in 50,000. No ill-effects are to be expected from the widespread use of iodine in such minute concentrations. The extra retail cost for iodized salt would, it is estimated, not exceed fourpence per head per annum. Iodized salt is already available by private purchase, and at present the supply is sufficient for the demand, because its use is still very restricted. Recently, the A and D vitamin tablets issued through the Ministry of Health for the use of expectant mothers have been fortified by the addition of a small amount of potassium iodide, so as to provide 100 μg. of iodine per tablet, that is per daily dose (Ministry of Health, 1947).

SUMMARY

1. During investigations on the distribution of dental fluorosis in England and Wales, goitre and thyroid enlargement were found to be prevalent in many districts, particularly rural areas. An enquiry into the distribution of such conditions and their association with the content of iodine and other minerals in the drinking water was then undertaken in connection with the promotion of a general scheme of iodine prophylaxis.

2. Consideration of methods used in previous surveys for the assessment of the size of the thyroid showed them to be unsuitable for the proposed investigations. In Part I of this report is outlined a method for the assessment of the state of the thyroid, in which simple clinical criteria are used. By the method described any gland can be placed in one of four categories (a) invisible at rest and on swallowing, (b) visible at rest, but soft, smooth and symmetrical, (c) more conspicuously visible but still soft, smooth and symmetrical (referred to as "visible +" or as the typical "Rossetti" neck), (d) visible and classified as pathological because either firm or nodular or asymmetrical.

3. A survey has been made covering 1,737 children, aged 11 to 15 years, in four areas of England served with waters of widely differing iodine content. The generally accepted inverse relation between incidence of thyroid enlargement and iodine content of the drinking water has been confirmed.

4. Similar surveys have also been made covering a wider area of England and certain areas in Scotland. These have included nearly 4,000 children aged 11 to 17 years. The incidence of thyroid enlargement was greater in some areas of England, and less in some areas of Scotland, than would have been expected from the iodine content of the drinking water.

5. The incidence of thyroid enlargement, and the iodine content of the water in the areas surveyed, have been considered in relation to the degree of hardness of the water. The higher incidence of goitre and thyroid enlargement in certain areas of England, as compared with that in certain Scottish areas having waters of similar iodine content, might be attributed to the degree of hardness of these English waters in contrast to the softness of the Scottish waters.

6. Surveys of established goitre at all ages are generally impracticable, since, to be reliable, they must involve house-to-house visits. Surveys of adolescents in schools, employing a standard method of recording, are eminently practicable, and the incidence of cases of hyperplasia may be held to reflect the adequacy or inadequacy of available iodine in the drinking water of the localities concerned.

7. The investigations included a village survey in a goitrous area covering 575 persons of all ages. From the results it was possible to show the age distribution of "physiological" enlargement of the thyroid and of true goitre.

8. It is debatable whether clinical enlargement of the thyroid occurring in adolescence should ever be regarded as physiological; its incidence is high in goitrous and low iodine areas and very low in areas with waters of high iodine content. In areas other than those of high goitre endemicity the gland is invisible in more than 94 per cent. of those examined.

9. The aim of investigating the relation of endemic goitre to endemic fluorosis has not been attained, because in England few areas exist with waters of sufficiently high fluorine content.

10. Some fresh evidence is submitted showing the association of endemic cretinism and congenital deaf-mutism with high incidence of goitre. A brief discussion is given of hereditary and environmental factors influencing iodine requirements.

11. During the present investigations values have been obtained for the

iodine content of 81 samples of drinking waters from England and 64 from Scotland.

12. Prophylaxis against thyroid enlargement and goitre by the general use of iodized salt is desirable in Great Britain. The procedure recommended is the addition of either 1 part of potassium iodide to 100,000 parts of all salt (NaCl), or 1 part to 40,000 parts of packeted table salt.

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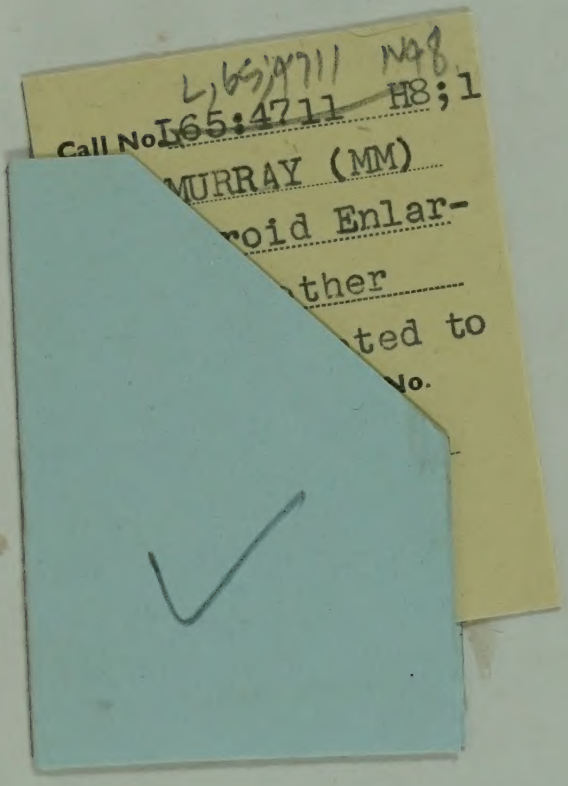
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